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(54) **DRUG DELIVERY AND GENE THERAPY DELIVERY SYSTEM**

WIRSTOFFABGABE UND GENTHERAPIESYSTEM

SYSTEME DE DELIVRANCE DE MEDICAMENT ET DE THERAPIE GENIQUE

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Description

1. Field of the Invention

[0001] The present invention relates generally to a drug or gene therapy delivery system.

2. Description of the Prior Art

[0002] The use of balloon catheters to administer medicaments to a patient is well known in the art. However, current devices suffer a drawback in that drug/gene solutions contained in coatings must be placed in contact with the artery wall for a long period of time. In this connection, the balloon must be inflated for a long duration, which can occlude blood flow. The actual quantity of drug/gene solution transfer to the anatomy of the artery is still unknown. Some of the drug/gene solution is believed to be washed downstream by the blood flow.

[0003] Examples of such arrangements are disclosed in U.S. patent Nos. 4,186,745 ("the '745 Patent"), 5,397,307 ("the '307 Patent"), and 5,547,472 ("the '472 Patent") and 5,674,192 ("the '192 Patent"). The '745 Patent teaches a catheter having a micropore structure over a portion of the catheter which permits the controlled release of substances such as sterile water, antiseptics, antibiotics, enzymes, and the like. The substances are released by differential thermal expansion of the catheter caused by contact with the patient.

[0004] The '307 Patent discloses an intravascular material delivery dilation catheter having a pair of spaced inflatable balloons defining a drug delivery region therebetween. One of the balloons is contoured to define fluid comminication paths when inflated. The other balloon has four lobes which are separated by grooves, which in combination with the inner wall of a blood vessel form fluid communication paths. Upon inflation of both balloons in the blood vessel, a medicament is injected via a drug delivery region between the inflated balloons, and flows past the distal balloon at a selected rate.

[0005] The '472 Patent teaches a balloon catheter including a tube or balloon provided with a plurality of pores, and a stimulus-responsive polymer attached to the pores such that fluid transmission through the pores is con trollable by a stimulus change, such as, for example, a change in pH, composition, and temperature. The catheter can administer a limited amount of medicament to a locally limited site only when necessary.

[0006] The '192 Patent discloses a catheter having an expandable portion with an exterior surface defined by a coating of a swellable hydrogel polymer. An aqueous solution of a drug to be delivered to the wall of a body lumen is incorporated into the hydrogel polymer. Compression of the coating against the lumen wall causes release of the drug when the expandable portion is expanded.

[0007] US Patent No. 5102402 discloses a balloon catheter to which microcapsules of a drug to be delivered have been attached. WO 95/03083 discloses a balloon catheter with an expandable portion that is defined by a hydrogel polymer within which an aqueous solution of a drug to be delivered is provided.

[0008] Similar disadvantages are exhibited by stents which include a drug-containing coating. One such stent is disclosed in EP 0 747 069.

[0009] In view of the foregoing, there exists a need for a new type of drug/gene therapy delivery system.

SUMMARY OF THE INVENTION

[0010] In accordance with one aspect of the present invention there is provided a delivery system as claimed in claim 1. A preferred feature of this aspect is set out in claim 2.

[0011] An advantage of an embodiment of the present invention is that it can provide a drug delivery and gene therapy delivery system which can be utilized in all urological applications, but which is not limited to such applications.

[0012] Another advantage of an embodiment of the present invention is that it can provide a drug delivery and gene therapy delivery system in accordance with the foregoing which can be configured for use with a stent.

[0013] Further advantages will become apparent hereinafter.

BRIEF DESCRIPTION OF DRAWINGS

[0014] Illustrative embodiments of the present invention will now be described, by way of example, with particular reference to the accompanying drawings, in which:

FIG. 1 is a sectional view of a balloon catheter and balloon in accordance with an arrangement that is outside the scope of the invention;

FIG. 2 is a sectional view of a balloon and balloon catheter in accordance with an arrangement which is outside the scope of the invention, the balloon and catheter being inserted into an artery of the patient with the balloon inflated to cause the microencapsulated spheres to become embedded in the wall of the artery;

FIG. 3 is a sectional view of a balloon and balloon catheter having extruded microencapsulated spheres in accordance with another arrangement that is also outside the scope of the invention; and

FIG. 4 is a sectional view of a radially expandable stent, coated with a plurality of microencapsulated spheres, in accordance with an embodiment of the

invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0015] With reference to the several views of the drawings there is shown a drug delivery and gene therapy system 10 in one implementation which is outside of the scope of the invention, and in which microencapsulated spheres generally denoted by the reference numeral 12 are disposed on the exterior of or extruded within the wall of a balloon 14 associated with a balloon catheter 16. The balloon catheter 16 and balloon 14 are conventional and well known in the art. The balloon catheter 16 is surgically or percutaneously inserted into an artery of the patient. The balloon catheter 16 may be coupled to an external shuttle gas source (not shown) to inflate and deflate the balloon 14.

[0016] Referring to FIG. 1, in an embodiment that is outside of the scope of the invention, the balloon 14 is disposed proximal to or at the distal end 18 of the balloon catheter 16 in conventional fashion. The balloon 14 defines an interior chamber 20 communicating with a lumen 22 defined in the balloon catheter 16 to facilitate inflation and deflation thereof. The shuttle gas follows a flow passage from lumen 22 as shown by the arrows in FIG. 1. An inner lumen 23 is sized to permit a guidewire to pass therethrough. The balloon 14 includes an outer peripheral surface 24, on which a plurality of microencapsulated spheres 12 are impregnated in a coating material 26, which may be, but is not limited to, a hydrophilic material. The microencapsulated spheres 12 contain any available drugs or gene therapy solutions capable of breaking up clots, repairing or healing damaged arteries, and the like, and are immersed in the coating 26. In an alternative embodiment shown in FIG. 3, that is also outside the scope of the invention, the microencapsulated spheres 12 are extruded in the wall 28 of the balloon during the manufacturing process. The microencapsulated spheres 12 are made from a biologically inert material, which may be a polymeric material, but is not limited to a polymeric material, and are sized (on the order of 5μ but not limited to such size) and configured to rupture upon application of a predetermined pressure caused by inflating the balloon 14. The microencapsulated spheres 12 are fabricated with a quantity of medicament in accordance with known techniques. For example, these are described in articles entitled Intelligent Gels, Toyoichi Tanaka, Chemical & Engineering News, Page 26, June 9, 1997, and Double Wall Microspheres - Advanced Drug Delivery, R & D, Page 64, March 1994. The technology described in the R & D Article has been licensed by Alkermes, of Cambridge Mass. The density of microencapsulated spheres 12 in the coating 26 is a function of the size of the spheres, balloon surface area and desired quantity of medicament to be administered. The coating typically comprises a hydrophilic material, although other materials may be employed within the scope of the invention, and is on the order of about 5μ in thickness, but is not limited to such size.

[0017] This arrangement allows for the microspheres 12 to become embedded in an artery wall 30 when an initial pressure is communicated to the balloon 14 as depicted in FIG. 2, and to thereafter rupture upon further inflation of the balloon 14 to cause the medicament to be administered to the patient. The amount of pressure required is a function of the balloon geometry and material, as well as the configuration of the microencapsulated spheres 12. The arrangement allows for the delivery of the medicament to a specific area, without undesirable occlusion of blood flow or dilution of the medicament. It also reduces the amount of time required for the balloon 14 to remain inflated within the artery. The microencapsulated sphere contents are infused directly into the artery wall, and consequently the delivery is more effective.

[0018] In accordance with a preferred embodiment of the invention as depicted in FIG. 4, the microencapsulated spheres 12 are disposed in a coating 26 on the exterior surface 32 of a stent 34. The stent 34 is advanced into the patient using conventional techniques such as over a guiding catheter (not shown) with an advancing catheter or element. The exterior surface 32 of the stent 34 is coated with the microspheres 12 in accordance with the techniques described in the foregoing. The stent 34 includes a mechanism generally denoted at 36 for radially expanding the stent 34 to cause the microencapsulated spheres 12 to become embedded in the artery wall 30 and thereafter to rupture to release the drug or gene therapy solution in a manner analogous to the balloon arrangement described above.

[0019] The balloon described in the foregoing can be used in a method for administering a drug or gene therapy solution to a patient that comprises the steps of:

(a) advancing a balloon catheter 16 having a balloon 14 with a plurality of microencapsulated spheres 12 containing a drug or gene therapy solution into an artery of a patient to a desired administration site;

(b) inflating the balloon 14 to a first predetermined pressure sufficient to cause the microspheres 12 to become embedded in the artery;

(c) further inflating the balloon 14 to a second higher predetermined pressure sufficient to cause the microencapsulated spheres 12 to rupture and release the drug or gene therapy solution into the artery wall 30; and

(d) thereafter withdrawing the balloon catheter 16 from the artery.

[0020] The stent of the invention can be used in a method for administering a drug or gene therapy solu-

tion to a patient that comprises the steps of:

(a) advancing a stent 34 coated with a plurality of microspheres 12 containing a drug or gene therapy solution into an artery of a patient to a desired administration site;

(b) radially expanding the stent 34 by a first predetermined amount sufficient to cause the microencapsulated spheres 12 to become embedded in the artery; and

(c) further expanding the stent 34 by a second higher predetermined amount sufficient to cause the microencapsulated spheres 12 to rupture and release the drug or gene therapy solution into the artery wall 30.

[0021] The present invention has been shown and described in what are considered to be the most practical and preferred embodiments. It is anticipated, however, that departures may be made therefrom and that obvious modifications will occur to persons skilled in the art, which fall within the scope of the appended claims.

Claims

1. A drug or gene therapy solution delivery system including a stent (34) capable of radial expansion, **characterised in that** said stent (34) comprises:

   a plurality of microencapsulated spheres (12) containing a medicament, said microencapsulated spheres (12) being disposed about an exterior surface (32) of said stent (34) so as to rupture upon radial expansion of said stent by a predetermined amount.

2. The system recited in Claim 1, wherein said microencapsulated spheres (12) are encapsulated in a coating (26) applied to said exterior surface (32) of said stent (34).

Patentansprüche

1. Wirkstoff- oder Gentherapielösungsabgabesystem, das einen Stent (34) enthält, der radial aufgeweitet werden kann, **dadurch gekennzeichnet, dass** der Stent (34) umfasst:

   eine Vielzahl mikroverkapselter Bereiche (12), die ein Medikament enthalten, wobei die mikroverkapselten Bereiche (12) so über einer äußeren Oberfläche (32) des Stents (34) angeordnet sind, dass sie bei einer radialen Aufweitung des Stents um einen vorbestimmten Betrag zerreißen.

2. System nach Anspruch 1, wobei die mikroverkapselten Bereiche (12) in einer Beschichtung (26) verkapselt sind, die auf die äußere Oberfläche (32) des Stents (34) aufgebracht ist.

Revendications

1. Système d'administration d'une solution médicamenteuse ou de thérapie génétique comprenant un stent (34) pouvant s'allonger radialement, **caractérisé en ce que** ledit stent (34) comprend:

   une pluralité de sphères micro - encapsulées (12) contenant un médicament, lesdites sphères micro - encapsulées (12) étant disposées autour d'une surface extérieure (32) dudit stent (34) de façon à se rompre lorsque ledit stent s'allonge radialement d'une longueur prédéterminée.

2. Système selon la revendication 1, dans lequel lesdites sphères micro - encapsulées (12) sont encapsulées dans un revêtement (26) appliqué sur ladite surface extérieure (32) dudit stent (34).

FIG. 1

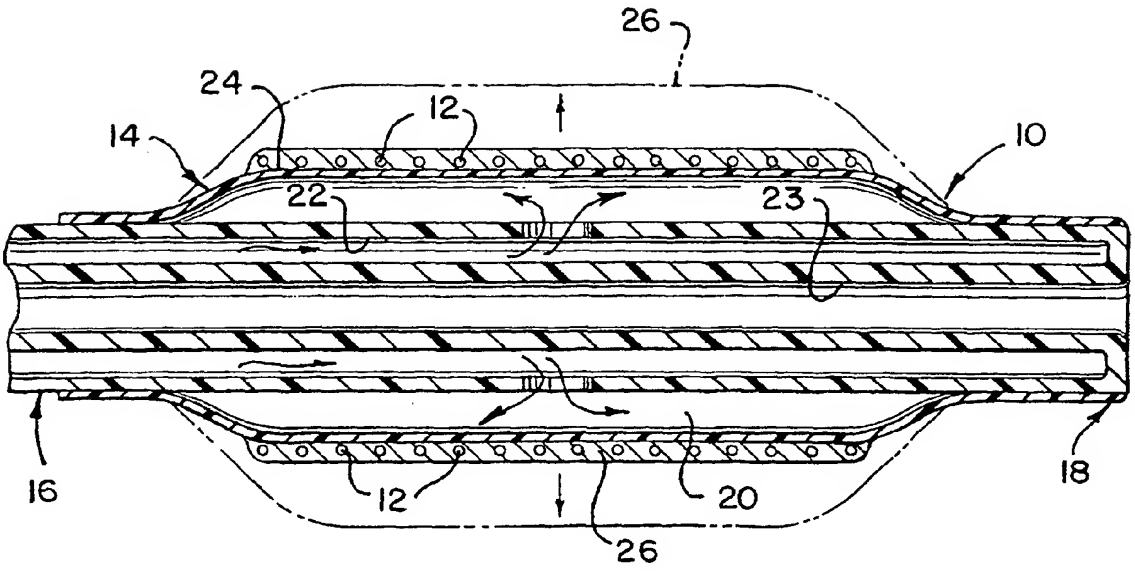

FIG. 2

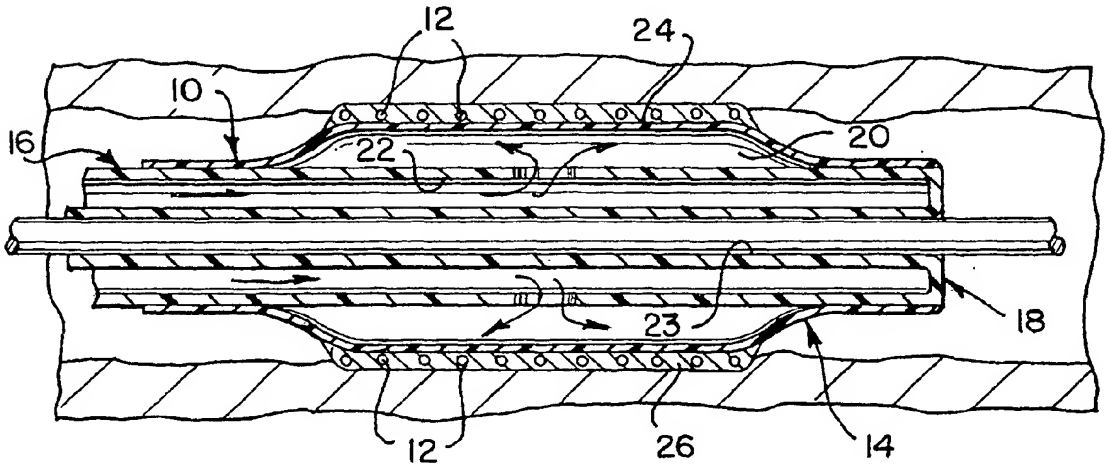

FIG. 3

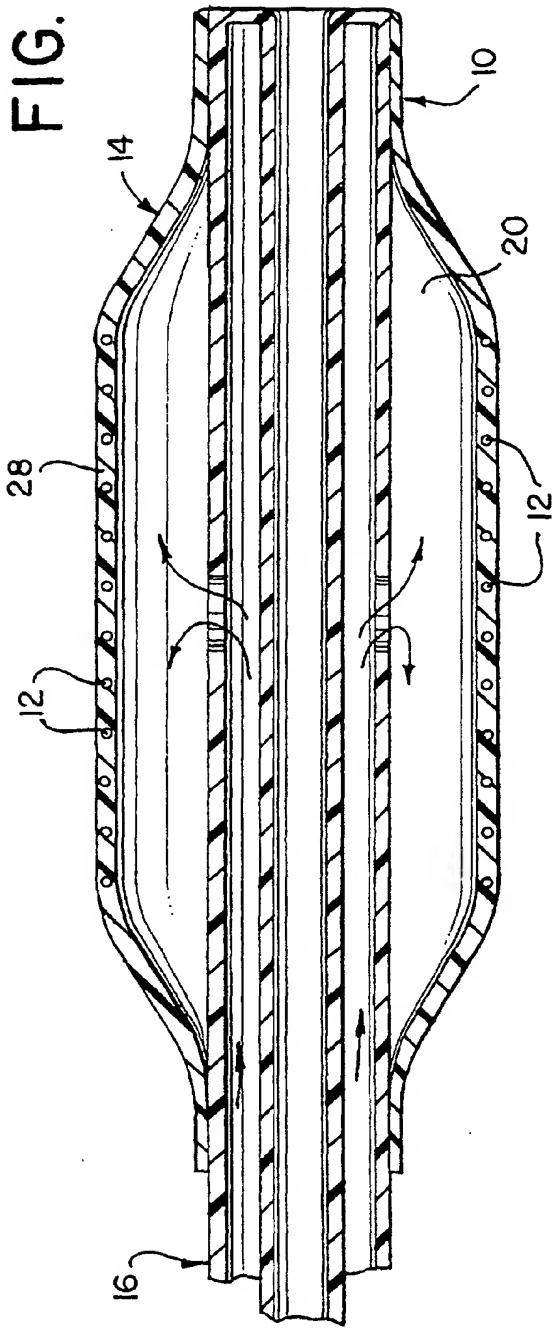

FIG. 4